

# Scalable, enantioselective taxane total synthesis

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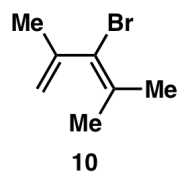
## SUPPORTING INFORMATION

### Part 1: Experimental Procedures and Characterisation Data

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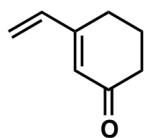
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**General Experimental.** All reactions were carried out under an inert nitrogen atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry acetonitrile (MeCN), dichloromethane (DCM), diethyl ether (Et<sub>2</sub>O), tetrahydrofuran (THF), toluene (PhMe) and triethylamine (Et<sub>3</sub>N) were obtained by passing the previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (<sup>1</sup>H-NMR) homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light as the visualising agent and an acidic solution of *p*-anisaldehyde and heat, ceric ammonium molybdate and heat, or KMnO<sub>4</sub> and heat as developing agents. Flash silica gel chromatography was performed using E. Merck silica gel (60, particle size 0.043–0.063 mm), flash alumina chromatography was performed using Brockmann Grade 1 aluminum oxide (activated, basic, 58 Å, 60 mesh powder), and flash Florisil<sup>®</sup> chromatography was conducted using Acros magnesium silicate (activated, 60–100 mesh). Chiral HPLC was performed using a Hitachi LaChrom Elite HPLC system. NMR spectra were recorded on Bruker DRX-600 and AMX-400 instruments and were calibrated using residual undeuterated solvent as an internal reference (CHCl<sub>3</sub> @ 7.26 ppm <sup>1</sup>H-NMR, 77.16 ppm <sup>13</sup>C-NMR). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionisation time-of-flight (ESI-TOF) reflectron experiments. IR experiments were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. Optical rotations were obtained on a Perkin-Elmer 341 polarimeter. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus and are uncorrected.



**Bromodiene 10.** Two-step procedures of **10** that are described in Magnus *et al.*, *Tetrahedron* **1999**, 55, 6435–6452 and in Fallis *et al.*, *Can. J. Chem.* **2004**, 82, 215–226 were modified such that this process was feasible in one pot. To a

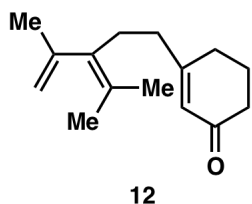
flame-dried 2 L round-bottomed flask equipped with a stir bar were added potassium *t*-butoxide (34.00 g, 303.0 mmol, 1.10 equiv), pentane or hexanes (400 mL), and 2,3-dimethyl-2-butene (60.00 mL, 42.48 g, 543.8 mmol, 1.98 equiv). The reaction flask was cooled to 0 °C and wrapped in aluminum foil, upon which freshly distilled bromoform (distilled over CaCl<sub>2</sub>; 24.00 mL, 69.36 g, 274.4 mmol, 1.00 equiv) was added in three equal portions over the course of 1 h. After the addition was complete, the reaction flask was removed from the ice-water bath and was warmed to room temperature over 2 h. The volatile components of this reaction mixture were then evaporated off *in vacuo*, upon which *N,N*-dimethylaniline (150 mL, 143.4 g, 1183.3 mmol, 4.31 equiv) was added. A reflux condenser was placed atop the reaction flask, and this reaction setup was placed in a 150 °C oil bath. The homogeneous reaction mixture was heated at 150 °C for 20 min, upon which it was cooled to room temperature. Et<sub>2</sub>O (800 mL) and aqueous hydrochloric acid (3 N; 400 mL) were then added. The phases were separated, and the organic phase was washed with additional hydrochloric acid (3 N; 2 × 400 mL), followed by water (400 mL) and brine (400 mL). It was then dried over anhydrous MgSO<sub>4</sub>, filtered, and concentrated *in vacuo* to yield a yellow liquid, which was pure by <sup>1</sup>H NMR analysis. However, further purification via filtration through an alumina plug rendered the product into a very slightly yellow, nonviscous liquid (32.0 g, 66.6 %). The spectroscopic data for this compound were identical to those reported in Fallis' report.



11

**Vinylcyclohexenone 11.** This compound was synthesised and characterised previously by Loughlin and co-workers: *Tetrahedron* **2007**, 63, 1395–1401. They

have noted that this compound “decomposed upon standing”, and we have also found that, when stored neat, this compound decomposes quickly even at  $-20\text{ }^{\circ}\text{C}$ , since adding  $\text{Et}_2\text{O}$  after prolonged storage results in a visual formation of white, insoluble solid (addition of THF or DCM does not cause such precipitation, however). This compound should be carried on immediately to the next step whenever possible; if prolonged storage is necessary, it is advisable that it be stored as a dilute solution in PhMe.



12

**Enone 12.** To a flame-dried 2 L round-bottomed flask equipped with a stir bar were added bromodiene **10** (16.00 g, 91.39 mmol, 1.27 equiv) and  $\text{Et}_2\text{O}$  (350 mL). This solution was cooled to  $-78\text{ }^{\circ}\text{C}$ , upon which *sec*-

butyllithium (1.4 M in cyclohexane; 60.0 mL, 84 mmol, 1.17 equiv) was added dropwise via syringe over 5 min. The resulting yellow solution was then stirred for 15 min at  $-78\text{ }^{\circ}\text{C}$ , and then the rubber septum atop the flask was briefly removed to introduce  $\text{CuBr}\cdot\text{SMe}_2$  (17.50 g, 85.12 mmol, 1.18 equiv). This bright yellow slurry was then stirred for 30 min at  $-78\text{ }^{\circ}\text{C}$ , after which freshly distilled chlorotrimethylsilane (distilled from  $\text{CaH}_2$ ; 18.00 mL, 15.41 g, 141.8 mmol, 1.97 equiv) was added dropwise over 5 min. After stirring for an additional 5 min at  $-78\text{ }^{\circ}\text{C}$ , a solution of vinylcyclohexenone **11** (8.800 g, 72.03 mmol, 1.00 equiv) in  $\text{Et}_2\text{O}$  (80 mL) was added dropwise over 10 min. During the addition, the reaction mixture became bright orange; it was stirred for 2 h at  $-78\text{ }^{\circ}\text{C}$  and was then allowed to warm to room temperature slowly, over 8 h, by removing the dry ice/acetone bath. The reaction mixture at this point appeared to be a dark slurry. To quench the reaction, this slurry was poured into a 3 L Erlenmeyer flask containing

glacial acetic acid (200 mL) and Et<sub>2</sub>O (800 mL), and was stirred for 30 min at room temperature. A further addition of hydrochloric acid (3 N; 500 mL) and stirring vigorously for 30 min at room temperature ensured the quenching of all alkaline species in the crude product. The two resulting layers were separated, and the aqueous layer was extracted twice with Et<sub>2</sub>O (2 × 300 mL). All the organic layers were combined in a 4 L Erlenmeyer flask, and saturated NaHCO<sub>3</sub> solution (total of 600 mL) was added in portions while stirring vigorously. The layers were then separated, and the organic layer was then washed with water (600 mL) followed by brine (400 mL), and dried over MgSO<sub>4</sub>. Evaporation *in vacuo* resulted in a dark yellow, viscous liquid (ca. 15 g). Column chromatography (SiO<sub>2</sub>, 1:40 to 1:3 EtOAc/hexanes) provided a light yellow, slightly viscous liquid (13.50 g, 85.8 %).

**Appearance:** Yellow liquid

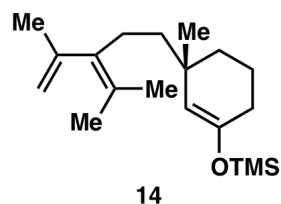
**TLC:**  $R_f$  = 0.45 (1:3 EtOAc/hexanes, UV active, stains dark blue upon *p*-anisaldehyde staining).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.88 (s, 1 H), 4.96 (dq,  $J$  = 3.0, 1.5 Hz, 1 H), 4.57 (dq,  $J$  = 2.7, 0.9 Hz, 1 H), 2.35 (t,  $J$  = 6.2 Hz, 2 H), 2.30 (t,  $J$  = 6.2 Hz, 2 H), 2.28 – 2.18 (m, 4 H), 1.98 (quintet,  $J$  = 6.2 Hz, 2 H), 1.76 (dd,  $J$  = 1.5, 0.9 Hz, 3 H), 1.67 (s, 6 H) ppm.

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>): δ 200.1, 166.8, 145.9, 135.2, 126.4, 125.7, 114.0, 37.5, 36.9, 30.0, 28.6, 22.9, 22.7, 21.9, 19.7 ppm.

**IR** (neat):  $\tilde{\nu}$  = 3074, 2924, 2867, 1667 ( $\tilde{\nu}_{\text{max}}$ ), 1625, 1444, 1429, 1371, 1346, 1324, 1251, 1191, 1132, 965, 888 cm<sup>-1</sup>.

**HRMS** (ESI-TOF): calc'd for C<sub>15</sub>H<sub>22</sub>O [ $M + H^+$ ] 219.1743, found 219.1746.



**(±)-TMS enol ether 14.** To a flame-dried 250 mL round-bottomed flask equipped with a stir bar were added copper (I) bromide dimethyl sulfide complex (130.0 mg, 0.632 mmol, 4.9 mol%) and THF (25 mL). This heterogeneous mixture was cooled to 0 °C, upon which trimethylaluminum solution (2.0 M in heptane; 7.60 mL, 15.2 mmol, 1.19 equiv) and a solution of enone **12** (2.8000 g, 12.820 mmol, 1.00 equiv) in THF (25 mL) were added successively, without any time between the two additions. The dark green-grey reaction mixture was then warmed to room temperature and stirred for 1 h. It was then cooled to 0 °C and then freshly distilled chlorotrimethylsilane (distilled from CaH<sub>2</sub>; 2.80 mL, 2.40 g, 22.1 mmol, 1.72 equiv) was added dropwise. This dark green slurry was then warmed to room temperature and stirred for 10 h. After this time, the black reaction mixture was cooled to 0 °C, and was poured onto a pre-cooled (0 °C) 2 L Erlenmeyer flask containing Florisil<sup>®</sup> (60 g), Et<sub>3</sub>N (60 mL), and hexanes (540 mL). This white slurry was then vigorously stirred for 1 h at room temperature, after which it was filtered under vacuum and rinsed with hexanes (400 mL), then concentrated *in vacuo* to yield a yellow liquid. A Florisil<sup>®</sup> column (60 g of Florisil<sup>®</sup>; elution with hexanes only) then provided a colourless, nonviscous liquid (3.10 g, 79 %).

**Appearance:** Colourless liquid

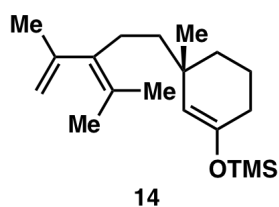
**TLC:**  $R_f$  = 0.20 (hexanes, slightly UV active but stains dark blue upon *p*-anisaldehyde staining).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 4.89 (dq,  $J$  = 2.9, 1.5 Hz, 1 H), 4.66 (s, 1 H), 4.53 (dq,  $J$  = 2.7, 1.0 Hz, 1 H), 2.09 – 1.97 (m, 2 H), 1.97 – 1.90 (m, 2 H), 1.75 (dd,  $J$  = 1.5, 1.0 Hz, 3 H), 1.72 – 1.62 (m, 2 H), 1.65 (s, 6 H), 1.47 – 1.37 (m, 1 H), 1.35 – 1.20 (m, 3 H), 0.95 (s, 3 H), 0.18 (s, 9 H) ppm.

**$^{13}\text{C}$  NMR** (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.5, 146.9, 137.2, 124.5, 114.4, 112.9, 41.9, 34.7, 34.6, 30.1, 28.1, 26.2, 22.9, 21.9, 19.8, 19.6, 0.5 ppm.

**IR** (neat):  $\tilde{\nu}$  = 3075, 2931, 2865, 1661, 1445, 1364, 1251, 1205, 1192, 1133, 963, 891, 862, 838 ( $\tilde{\nu}_{\text{max}}$ ),  $750\text{ cm}^{-1}$ .

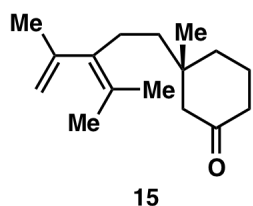
**HRMS** (ESI-TOF): calc'd for  $\text{C}_{19}\text{H}_{34}\text{OSi}$  [ $\text{M} + \text{H}^+$ ] 307.2452, found 307.2450.



**(-)-TMS enol ether 14.** The procedure for the “reverse” copper-catalyzed asymmetric conjugate addition to trisubstituted enones, as reported by Alexakis *et al.*, *Chem. Eur. J.* **2007**, *13*, 9647–9662 was followed. Although the authors state that silylation of the formed aluminum enolate was difficult, a modified quenching procedure described below allowed the TMS trap to occur in good and consistent yields. Thus, to a flame-dried 100 mL Schlenk flask equipped with a stir bar were added copper (I) 2-thiophenecarboxylate (17.4 mg, 0.0912 mmol, 2.0 mol%), ligand **13** (prepared according to Alexakis’ paper above; 90.8 mg, 0.183 mmol, 4.0 mol%;) and degassed  $\text{Et}_2\text{O}$  (10 mL). This solution was stirred for 30 min at room temperature, upon which it was cooled to  $-78\text{ }^\circ\text{C}$ , and a solution of enone **12** (1.000 g, 4.580 mmol, 1.00 equiv) in degassed  $\text{Et}_2\text{O}$  (10 mL) was added dropwise over 5 min. Immediately thereafter, trimethylaluminum solution (2.0 M in heptane; 3.20 mL, 6.40 mmol, 1.40 equiv) was added dropwise via syringe over 5 min. The resulting yellow solution was then stirred for 24 h at  $-30\text{ }^\circ\text{C}$  using a temperature-controlled bath, after which TLC showed complete consumption of starting material. THF (30 mL) was then added slowly over 1 min, followed by freshly distilled chlorotrimethylsilane (distilled over  $\text{CaH}_2$ ; 1.00 mL, 0.856 g, 7.879 mmol, 1.72 equiv). The reaction mixture was then slowly warmed to room temperature over 10 h by removing it from the cold bath. The reaction mixture

at this point appeared dark grey. Although TLC showed incomplete silylation at this point, this was a TLC artifact caused by the acidity of the reaction medium. The reaction flask was then cooled to 0 °C, and was poured onto a pre-cooled (0 °C) 2 L Erlenmeyer flask containing Florisil® (60 g), Et<sub>3</sub>N (60 mL), and hexanes (540 mL). This white slurry was then vigorously stirred for 1 h at room temperature, after which it was filtered under vacuum and rinsed with hexanes (400 mL), then concentrated *in vacuo* to yield a yellow liquid. A Florisil® column (60 g of Florisil®; elution with hexanes only) then provided a colourless, nonviscous liquid (1.255 g, 89 %). It is of note that this reaction could be run at the 5-gram scale, but a higher catalyst loading (4 mol% CuTC, 8 mol% ligand) would be necessary.

Its spectroscopic data was identical to that reported above for (±)-**14**, except for the optical rotation:  $[\alpha]_D^{20}$  (c 1.0, CHCl<sub>3</sub>) = -1.3°, taken on a 93% ee sample (see experimental details for the synthesis of (+)-**15** for the determination of enantioselectivity of this reaction.



**(±)-Ketone 15.** This compound was required in order to analyze the enantioselectivity of the asymmetric reaction, acting as the racemic mixture control sample with which to calibrate the chiral HPLC

experiment. It was formed via simple hydrolysis of (±)-TMS enol ether **14**: To a vial were added non-dry THF (2 mL), (±)-**14** (20 mg, 0.065 mmol), and aqueous hydrochloric acid (3 N; 1 mL), and this homogeneous reaction was stirred for 5 min at room temperature. Extraction with EtOAc (5 mL) and washing the resulting organic layer with water (3 mL) and brine (3 mL), followed by drying over MgSO<sub>4</sub>, filtration and evaporation *in vacuo*, provided (±)-**15** as a slightly yellow, nonviscous liquid (14.5 mg, 94.8 %).

**Appearance:** Slightly yellow liquid



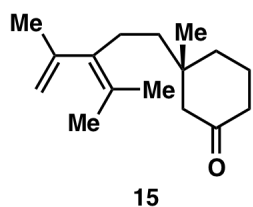
**TLC:**  $R_f$  = 0.63–0.66 (1:3 EtOAc/hexanes, slightly UV active but stains dark blue upon *p*-anisaldehyde staining).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.90 (dq,  $J$  = 3.0, 1.5 Hz, 1 H), 4.53 (dq,  $J$  = 2.7, 0.9 Hz, 1 H), 2.27 (t,  $J$  = 6.7 Hz, 2 H), 2.16 (AB quartet, apparent dd,  $J$  = 31.5, 13.0 Hz, 2 H), 2.01 (m, 2 H), 1.87 (m, 2 H), 1.74 (dd,  $J$  = 1.5, 0.9 Hz, 3 H), 1.65 (s, 3 H), 1.64 (s, 3 H), 1.59 (m, 2 H), 1.26 (m, 2 H), 0.93 (s, 3 H) ppm .

**$^{13}\text{C}$  NMR** (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  212.4, 146.5, 136.4, 125.2, 113.3, 53.9, 41.2, 40.2, 38.7, 35.8, 25.1, 24.9, 22.9, 22.3, 21.9, 19.6 ppm.

**IR** (neat)  $\tilde{\nu}$  = 3074, 2953, 2935, 2871, 1711 ( $\tilde{\nu}_{\text{max}}$ ), 1631, 1446, 1428, 1379, 1364, 1312, 1287, 1227, 1075, 891  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF): calc'd for  $\text{C}_{16}\text{H}_{26}\text{O}$  [ $\text{M} + \text{H}^+$ ] 235.2056, found 235.2059.



**(+)-Ketone 15.** This compound was required in order to analyze the enantioselectivity of the asymmetric reaction. It was formed via simple hydrolysis of (–)-TMS enol ether **14**, as reported above for (±)-**14**. Its

spectroscopic data was identical to that reported for (±)-**14**, with the exception of optical rotation,

$[\alpha]_D^{20}$  (c 1.0,  $\text{CHCl}_3$ ) = +0.8°, taken on a 93% ee sample.

Method for determining the enantioselectivity of the asymmetric conjugate addition, using (±)-**15** and (+)-**15**:

Column: Daicel Chiralcel<sup>®</sup> OJ

Dimensions: 4.6 × 250 mm

Eluent: 100% hexanes

Flow rate: 0.5 mL/min

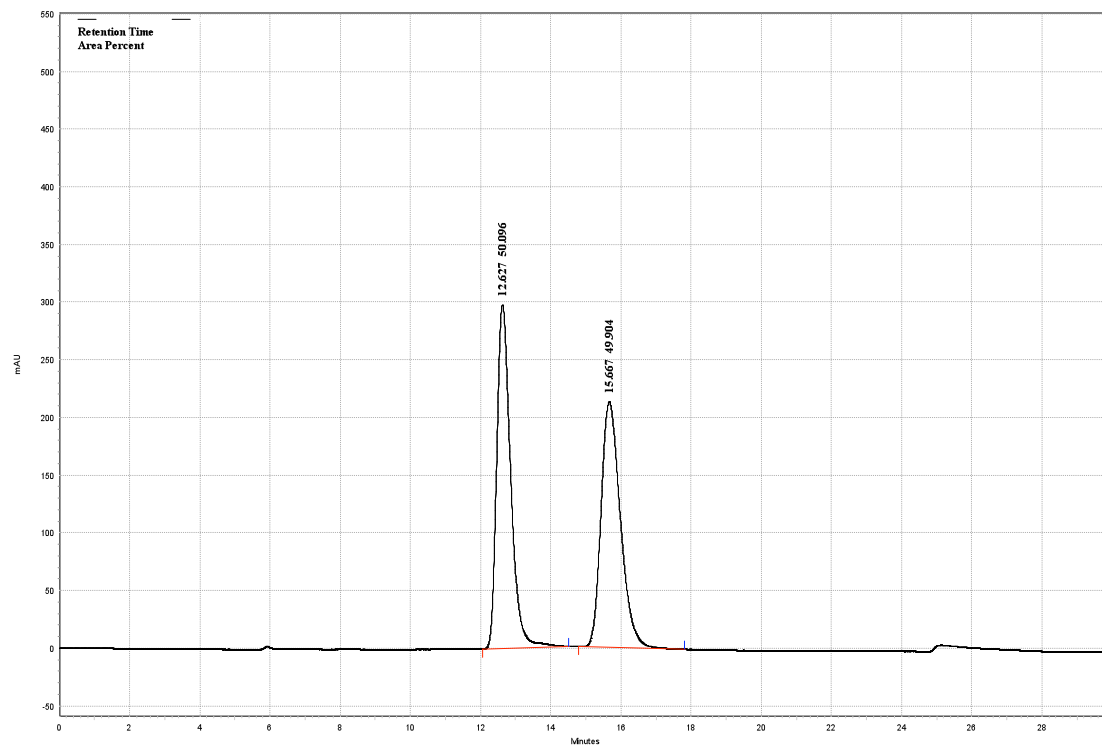


Figure S1. Chromatogram of (±)-**15** on a chiral column, showing ~0% ee.

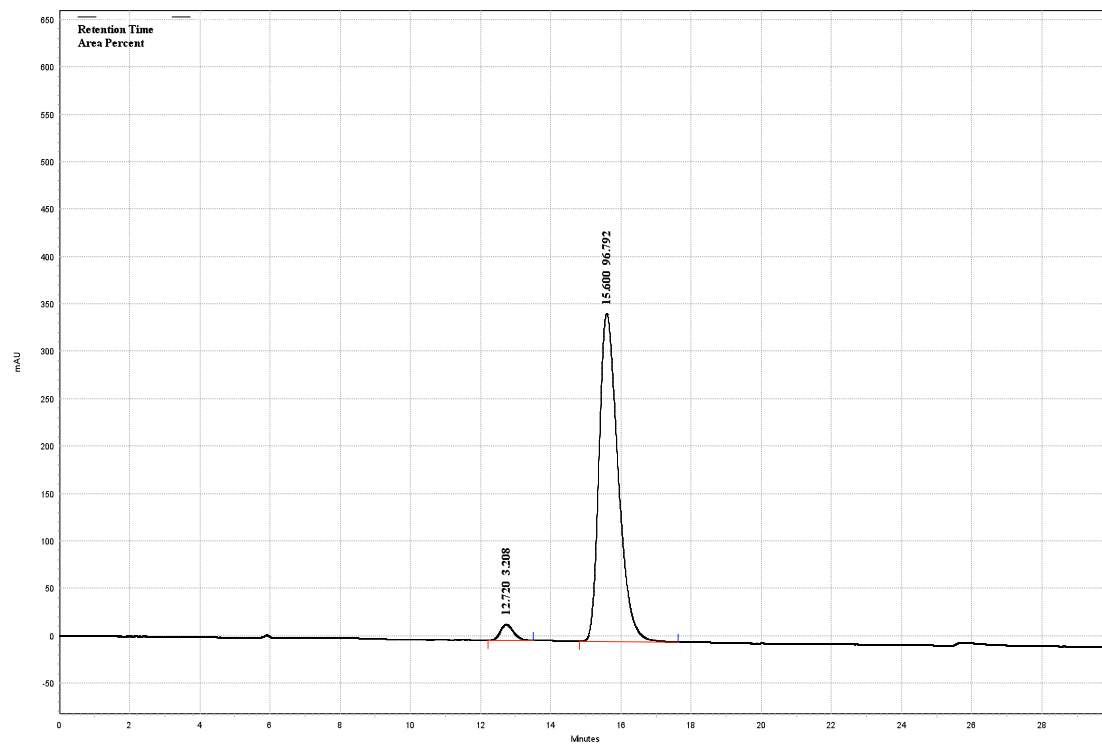


Figure S2. Chromatogram of (+)-**15** on a chiral column, showing 93.6% ee.

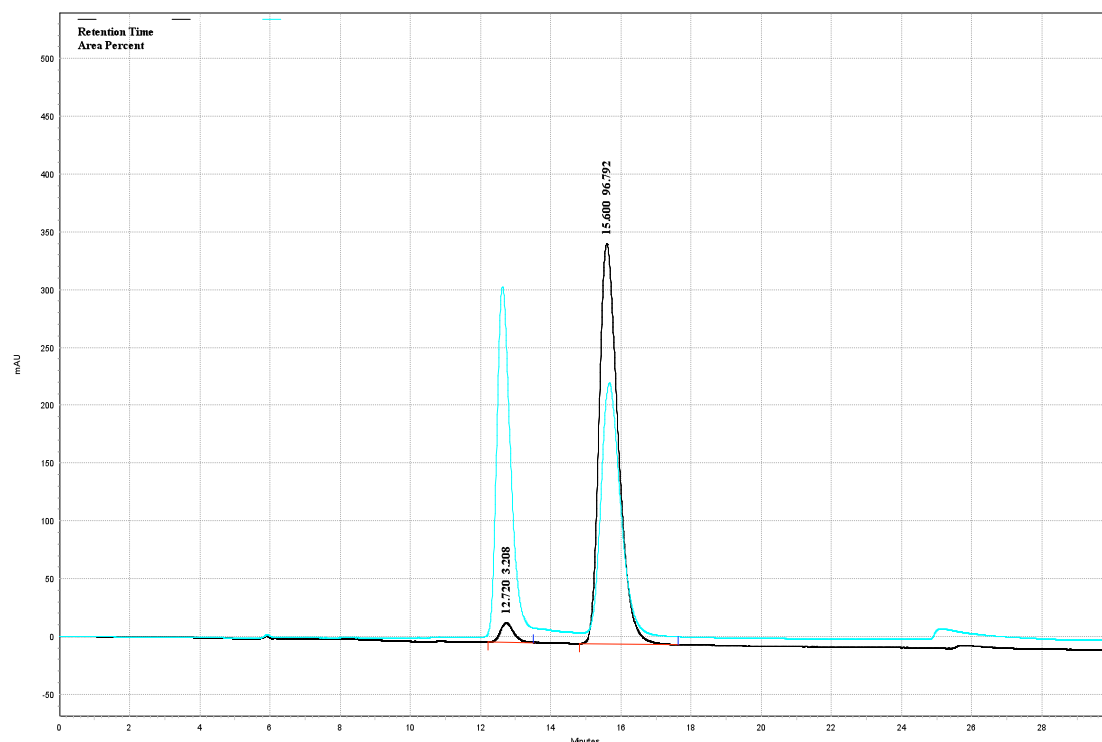
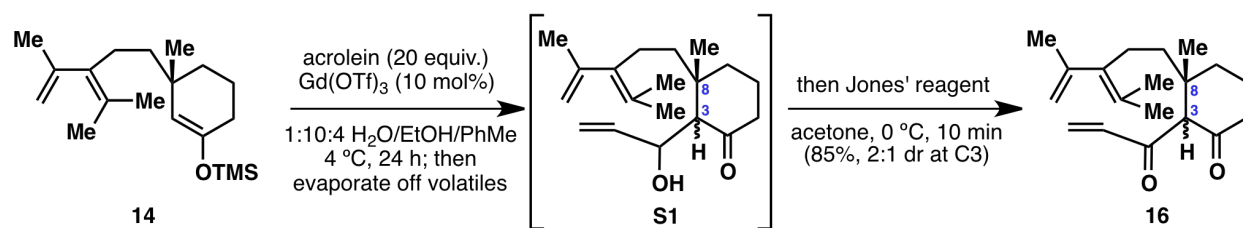


Figure S3. Overlaid chromatograms of (±)-**15** and (+)-**15**.



**Aldol Product S1 and Uncyclised Diketone 16.** The procedure for the lanthanide-catalysed aldol reaction using a ternary solvent, as reported by Kobayashi *et al.*, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2342–2344 was followed. Thus, to a flame-dried 250 mL round-bottomed flask equipped with a stir bar was added a solution of (–)-TMS enol ether **14** (3.170 g, 8.648 mmol, 1.00 equiv) in PhMe (15 mL) and was cooled to 0 °C. Freshly distilled acrolein (from CaSO<sub>4</sub>; 11.6 mL, 9.73 g, 173.6 mmol, 20.0 equiv) was added, followed by a solution of Gd(OTf)<sub>3</sub> (0.520 g, 0.860 mmol, 0.10 equiv) in 1:10 H<sub>2</sub>O/EtOH (41 mL). This colourless, homogeneous solution

was stirred in the cold room for 4 °C, after which most of the volatiles were removed via rotary evaporation over a short period of less than 10 min (CAUTION! The removal of volatiles should be done in a well-ventilated fumehood, since acrolein is removed).

At this point, intermediate **S1** could be worked up (by addition of 70 mL PhMe and washing with 50 mL H<sub>2</sub>O, 50 mL brine and drying over Na<sub>2</sub>SO<sub>4</sub>, followed by evaporation *in vacuo*) and purified (via basic alumina flash chromatography) to give an inseparable 2:1 mixture of diastereomers at C3, in a combined ca. 70% yield. However, it is more convenient to run the following oxidation reaction without workup as shown below.

Crude product **S1** without workup was immediately dissolved in 100 mL ‘non-dry’ acetone and was cooled to 0 °C. Jones’ reagent (20 mL, 2.1 M; made from 5.34 g CrO<sub>3</sub>, 4.6 mL conc. H<sub>2</sub>SO<sub>4</sub> and 20 mL H<sub>2</sub>O) was added dropwise and the reaction mixture was stirred at 0 °C for 10 min. It was then quenched with 10 mL isopropyl alcohol, and stirred for an additional 10 min at 0 °C. This dark green mixture was then transferred over to a separatory funnel, upon which 300 mL EtOAc and 300 mL H<sub>2</sub>O were added. The two layers were separated, and the aqueous layer was extracted with 2 × 200 mL EtOAc. The organic layers were combined, washed with 300 mL H<sub>2</sub>O and 300 mL brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated to dryness *in vacuo*. Purification via silica gel flash chromatography (gradient of EtOAc/hexanes) gave an inseparable 2:1 mixture of diastereomers at C3, along with 7–8 % w/w (+)-desilylated ketone **15**, in a combined ca. 94% yield (2.35 g), resulting in an approximate 85% yield.

Data for **S1** as a 2:1 mixture of diastereomers at C3:

**Appearance:** Colourless, viscous liquid

**TLC:**  $R_f$  = 0.35–0.39 (1:3 EtOAc/hexanes, very slightly UV active on TLC, stains dark blue upon *p*-anisaldehyde staining).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):

**(3R,8S)-S1** (major): δ 6.17 (ddd, *J* = 17.1, 10.1, 8.2 Hz, 1 H), 5.30 – 5.05 (m, 2 H), 4.92 (dq, *J* = 2.9, 1.5 Hz, 1 H), 4.54 (dq, *J* = 2.8, 0.9 Hz, 1 H), 4.29 (q, *J* = 6.6 Hz, 1 H), 2.69 (d, *J* = 4.9 Hz, 1 H), 2.63 (d, *J* = 8.0 Hz, 1 H), 2.40 – 2.20 (m, 2 H), 2.20 – 1.80 (m, 4 H), 1.75 (dd, *J* = 1.5, 0.9 Hz, 4 H), 1.66 (s, 3 H), 1.65 (s, 3 H), 1.60 – 1.20 (m, 2 H), 0.95 (s, 3 H) ppm.

**(3S,8S)-S1** (minor): δ 6.13 (ddd, *J* = 17.2, 10.2, 7.7 Hz, 1 H), 5.30 – 5.05 (m, 2 H), 4.88 (dq, *J* = 2.9, 1.5 Hz, 1 H), 4.50 (dq, *J* = 2.8, 0.9 Hz, 1 H), 4.38 (q, *J* = 6.4 Hz, 1 H), 2.58 (d, *J* = 5.2 Hz, 1 H), 2.49 (d, *J* = 7.2 Hz, 1 H), 2.40 – 2.20 (m, 2 H), 2.20 – 1.80 (m, 4 H), 1.72 (dd, *J* = 1.5, 0.9 Hz, 2 H), 1.62 (s, 3 H), 1.61 (s, 3 H), 1.60 – 1.20 (m, 2 H), 1.09 (s, 3 H) ppm.

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>):

**(3R,8S)-S1** (major): δ 214.4, 146.5, 139.5, 136.2, 125.3, 117.4, 113.4, 72.2, 63.6, 41.8, 40.9, 39.3, 36.4, 25.8, 24.9, 22.9, 21.8, 21.8, 19.6 ppm;

**(3S,8S)-S1** (minor): δ 213.8, 146.6, 139.9, 136.4, 125.0, 116.8, 113.2, 72.0, 66.8, 41.9, 41.2, 35.5, 33.8, 25.8, 25.1, 22.9, 21.8, 21.7, 19.6 ppm;

**IR** (neat)  $\tilde{\nu}$  = 3440, 3075, 2935, 2874, 1699, 1631, 1444, 1372, 1309, 1266, 998, 925, 894, 735 ( $\tilde{\nu}_{\text{max}}$ ), 703 cm<sup>-1</sup>.

**HRMS** (ESI-TOF): calc'd for C<sub>19</sub>H<sub>30</sub>O<sub>2</sub> [M + H<sup>+</sup>] 291.2318, found 291.2314.

Data for **16** as a 2:1 mixture of diastereomers at C3:

**Appearance:** Yellow liquid

**TLC:** *R<sub>f</sub>* = 0.65–0.69 (1:3 EtOAc/hexanes, slightly UV active on TLC, stains dark blue upon *p*-anisaldehyde staining).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):

**(3S,8S)-16** (major): δ 6.35 (d, *J* = 10.2 Hz, 1 H), 6.24 (d, *J* = 17.4, 1.0 Hz, 1 H), 5.80 (d, *J* =

10.3, 1.1 Hz, 1 H), 4.90 (dq,  $J = 3.0, 1.5$  Hz, 1 H), 4.52 (dq,  $J = 2.7, 0.9$  Hz, 1 H), 3.76 (t,  $J = 1.2$  Hz, 1 H), 2.68 (ddd,  $J = 14.2, 10.6, 6.8$  Hz, 1 H), 2.35 – 2.25 (m, 1 H), 2.20 – 1.80 (m, 5 H), 1.73 (dd,  $J = 1.5, 0.9$  Hz, 3 H) 1.57 (s, 3 H), 1.55 – 1.45 (m, 1 H), 1.35 – 1.15 (m, 2 H), 0.99 (s, 3 H) ppm.

**(3R,8S)-16** (minor):  $\delta$  6.39 (d,  $J = 10.3$  Hz, 1 H), 6.28 (d,  $J = 17.4, 1.4$  Hz, 1 H), 5.82 (d,  $J = 10.0, 1.4$  Hz, 1 H), 4.87 (dq,  $J = 3.0, 1.5$  Hz, 1 H), 4.48 (dq,  $J = 2.7, 0.9$  Hz, 1 H), 3.78 (t,  $J = 1.4$  Hz, 1 H), 2.64 (ddd,  $J = 14.0, 12.2, 7.0$  Hz, 1 H), 2.35 – 2.25 (m, 1 H), 2.20 – 1.80 (m, 5 H), 1.69 (dd,  $J = 1.5, 0.9$  Hz, 3 H), 1.58 (s, 3 H), 1.55 – 1.45 (m, 1 H), 1.35 – 1.15 (m, 2 H), 0.95 (s, 3 H) ppm.

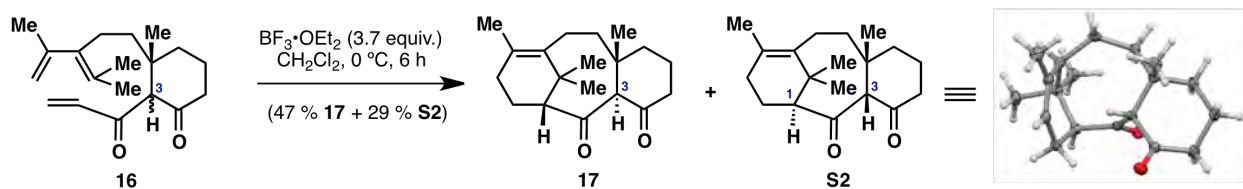
$^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ ):

**(3S,8S)-16** (major):  $\delta$  208.1, 196.6, 146.2, 137.9, 135.8, 129.3, 125.6, 113.6, 70.3, 42.1, 39.4, 37.8, 31.6, 24.7, 23.5, 22.8, 21.9, 21.6, 19.6 ppm;

**(3R,8S)-16** (minor):  $\delta$  207.8, 196.1, 146.2, 137.5, 136.0, 129.7, 125.4, 113.5, 71.3, 42.6, 39.0, 38.2, 32.3, 25.1, 24.0, 22.9, 22.1, 21.9, 19.6 ppm;

**IR** (neat)  $\tilde{\nu} = 3074, 2929, 2874, 1708, 1684, 1669, 1608, 1446, 1380, 1267, 1070, 983, 894, 735$  ( $\tilde{\nu}_{\text{max}}$ ),  $702\text{ cm}^{-1}$ .

**HRMS** (ESI-TOF): calc'd for  $\text{C}_{19}\text{H}_{28}\text{O}_2$  [ $\text{M} + \text{H}^+$ ] 289.2162, found 289.2165.



**Cyclised Diketone (+)-17 and Diastereomeric Diketone (–)-S2.** The procedure for the  $\text{BF}_3 \cdot \text{OEt}_2$ -promoted Diels–Alder reaction, as reported by Williams *et al.*, *J. Org. Chem.* **2000**, 65, 7865–7869 was modified as follows. Thus, to a flame-dried 1 L two-necked round-bottomed

flask equipped with a stir bar and an additional funnel were added  $\text{BF}_3 \cdot \text{OEt}_2$  (3.60 mL, 4.14 g, 29.2 mmol, 3.65 equiv) and 500 mL  $\text{CH}_2\text{Cl}_2$ . The round-bottomed flask portion was cooled to 0 °C, and a dry solution of **16** (as a mixture of **16** and **15**; containing a 2:1 mixture of C3-isomers in a total of 2.31 g, 8.01 mmol, 1.00 equiv) in  $\text{CH}_2\text{Cl}_2$  (125 mL) was cannulated into the addition funnel. This uncyclised diketone solution was added to the  $\text{BF}_3 \cdot \text{OEt}_2$  solution dropwise, very slowly, over 5 h. After the addition was complete, the addition funnel was rinsed with 5 mL  $\text{CH}_2\text{Cl}_2$  and this rinsate was transferred to the reaction flask as well. The yellow-orange, homogeneous reaction mixture was stirred for an additional 1 h at 0 °C, after which it was quenched by pouring into a 2 L Erlenmeyer flask containing cold  $\text{NaHCO}_3$  solution (500 mL, aqueous, saturated). This mixture was poured into a 3 L separatory funnel and the layers were separated. The aqueous layer was extracted with 2 × 300 mL  $\text{CH}_2\text{Cl}_2$ . The organic layers were combined, washed with 400 mL  $\text{H}_2\text{O}$  and 400 mL brine, dried over  $\text{Na}_2\text{SO}_4$  and evaporated to dryness *in vacuo*. Purification via silica gel flash chromatography (gradient of EtOAc/hexanes) gave 0.862 g of (–)-**S2** and (+)-**15** as a 2.8:1.0 molar mixture eluting first, followed by 1.079 g of pure (+)-**17** eluting thereafter. Yields: 1.079 g (+)-**17** (46.7 %) + 0.668 g (–)-**S2** (28.9 %).

Data for (+)-**17**:

**Appearance:** Yellow, viscous liquid that solidifies upon standing to a beige, amorphous solid.

**TLC:**  $R_f$  = 0.45–0.48 (1:3 EtOAc/hexanes, very slightly UV active but stains orange upon *p*-anisaldehyde staining).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.19 (s, 1 H), 2.87 (ddd,  $J$  = 14.3, 12.2, 5.4 Hz, 1 H), 2.56 – 2.42 (m, 1 H), 2.41 (d,  $J$  = 8.4 Hz, 1 H), 2.37 – 2.28 (m, 1 H), 2.22 – 2.10 (m, 2 H), 2.06 – 1.86 (m, 5 H), 1.88 (s, 3 H), 1.72 (ddd,  $J$  = 15.4, 12.2, 5.2 Hz, 1 H), 1.63 (ddd,  $J$  = 15.7, 10.1, 5.9 Hz, 1 H),

1.41 (ddd,  $J = 15.4, 5.4, 4.1$  Hz, 1 H), 1.37 – 1.29 (m, 1 H), 1.22 (s, 3 H), 1.08 (s, 3 H), 0.98 (s, 3 H) ppm.

**$^{13}\text{C}$  NMR** (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  210.0, 206.9, 137.1, 131.5, 64.0, 61.9, 44.1, 39.5, 39.4, 38.4, 37.5, 29.5, 28.9, 25.4, 25.0, 24.1, 22.3, 21.1, 17.9 ppm.

**IR** (neat):  $\tilde{\nu} = 2923, 2899, 1721$  ( $\tilde{\nu}_{\text{max}}$ ), 1688, 1553, 1458, 1381, 1352, 1336, 1262, 1235, 1166, 1132, 1049, 966  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF): calc'd for  $\text{C}_{19}\text{H}_{28}\text{O}_2$  [ $\text{M} + \text{H}^+$ ] 289.2162, found 289.2162.

**Optical rotation:**  $[\alpha]_D^{20}$  (c 1.0,  $\text{CHCl}_3$ ) = +106°, taken on a 93% ee sample.

Data for (–)-**S2**:

**Appearance:** Yellow liquid that solidifies upon standing to a white, crystalline solid.

**Melting point:** 160–165 °C

**TLC:**  $R_f = 0.65$ – $0.67$  (1:3 EtOAc/hexanes, very slightly UV active but stains orange upon *p*-anisaldehyde staining).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.67 (s, 1 H), 2.86 (td,  $J = 13.9, 7.1$  Hz, 1 H), 2.81 (td,  $J = 13.6, 5.4$  Hz, 1 H), 2.55 – 2.39 (m, 1 H), 2.43 (d,  $J = 7.3$  Hz, 1 H), 2.29 – 2.19 (m, 2 H), 2.16 – 2.06 (m, 2 H), 2.05 – 1.85 (m, 4 H), 1.85 (s, 3 H), 1.82 – 1.67 (m, 1 H), 1.31 (dd,  $J = 5.4, 2.5$  Hz, 1 H), 1.28 (s, 3 H), 1.17 – 1.12 (m, 1 H), 1.11 (s, 3 H), 0.96 (s, 3 H) ppm.

**$^{13}\text{C}$  NMR** (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  211.0, 209.6, 136.2, 131.7, 69.1, 62.6, 43.7, 40.0, 39.4, 38.4, 35.9, 29.6, 28.8, 25.0, 24.8, 24.3, 22.1, 21.2, 17.9 ppm.

**IR** (neat):  $\tilde{\nu} = 2920, 1705, 1678$  ( $\tilde{\nu}_{\text{max}}$ ), 1457, 1390, 1314, 1264, 1220, 1166, 1131, 1113, 1030, 968, 943, 894  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF): calc'd for  $\text{C}_{19}\text{H}_{28}\text{O}_2$  [ $\text{M} + \text{H}^+$ ] 289.2162, found 289.2166.

**Optical rotation:**  $[\alpha]_D^{20}$  (c 0.4,  $\text{CHCl}_3$ ) = +252°, taken on a 93% ee sample.



X-ray crystallographic data for (-)-**S2**:

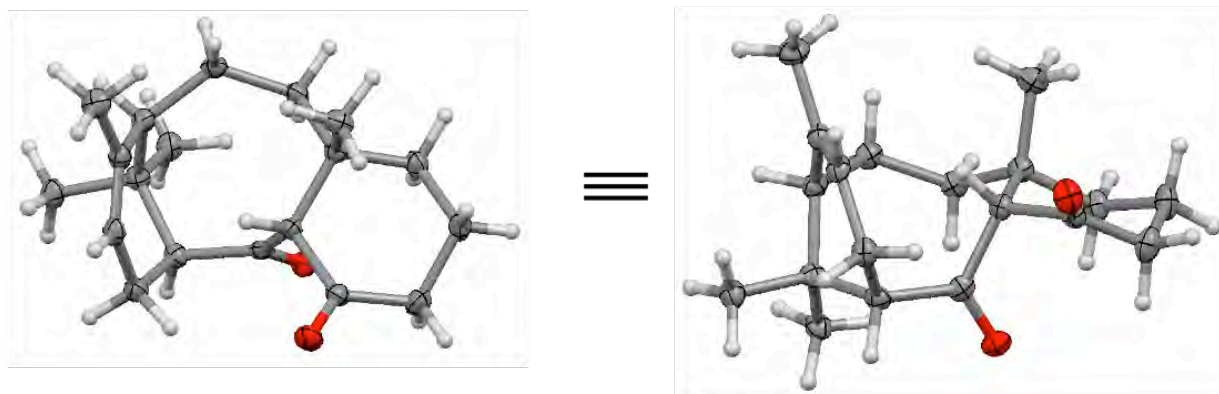


Table S1. Crystal data and structure refinement for CCDC # 840165.

Identification code	CCDC # 840165	
Empirical formula	C <sub>19</sub> H <sub>28</sub> O <sub>2</sub>	
Formula weight	288.41	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 7.7453(4) Å	α = 90°
	b = 10.3009(6) Å	β = 94.175(2)°
	c = 9.7366(5) Å	γ = 90°
Volume	774.76(7) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.236 g/cm <sup>3</sup>	
Absorption coefficient	0.603 mm <sup>-1</sup>	
F(000)	316	
Crystal size	0.40 x 0.36 x 0.08 mm <sup>3</sup>	
Theta range for data collection	4.55 to 68.09°	
Index ranges	-8 ≤ h ≤ 8, -11 ≤ k ≤ 11, -10 ≤ l ≤ 11	
Reflections collected	3966	
Independent reflections	1823 [R(int) = 0.0259]	
Completeness to theta = 66.00°	95.7 %	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9534 and 0.7946	

Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	1823 / 1 / 194
Goodness-of-fit on F <sup>2</sup>	1.162
Final R indices [I>2sigma(I)]	R1 = 0.0421, wR2 = 0.1018
R indices (all data)	R1 = 0.0422, wR2 = 0.1018
Absolute structure (Flack) parameter	0.1(2)
Largest diff. peak and hole	0.300 and -0.178 e Å <sup>-3</sup>

Table S2. Atomic coordinates (x 10<sup>4</sup>) and equivalent isotropic displacement parameters (Å<sup>2</sup> x 10<sup>3</sup>) for CCDC # 840165. U(eq) is defined as one third of the trace of the orthogonalised U<sup>ij</sup> tensor.

	x	y	z	U(eq)
O(1)	11102(2)	11123(2)	3964(1)	26(1)
O(2)	7511(2)	11975(1)	1091(1)	23(1)
C(1)	9595(2)	11433(2)	3732(2)	21(1)
C(2)	8338(2)	10509(2)	2940(2)	18(1)
C(3)	8110(2)	10921(2)	1422(2)	19(1)
C(4)	8705(2)	9985(2)	341(2)	20(1)
C(5)	10388(2)	9270(2)	845(2)	21(1)
C(6)	10071(2)	8035(2)	1610(2)	21(1)
C(7)	8511(2)	7502(2)	1737(2)	21(1)
C(8)	8349(2)	6252(2)	2531(2)	27(1)
C(9)	6554(2)	10388(2)	3590(2)	19(1)
C(10)	6851(2)	9545(2)	4890(2)	24(1)
C(11)	5887(2)	11739(2)	3978(2)	24(1)
C(12)	7192(3)	12513(2)	4897(2)	28(1)
C(13)	8882(3)	12707(2)	4189(2)	28(1)
C(14)	5175(2)	9779(2)	2563(2)	20(1)
C(15)	5409(2)	8409(2)	1956(2)	21(1)
C(16)	6868(2)	8032(2)	1000(2)	20(1)
C(17)	7288(2)	8982(2)	-177(2)	20(1)
C(18)	8027(2)	8175(2)	-1328(2)	24(1)
C(19)	5669(2)	9662(2)	-833(2)	23(1)

Table S3. Bond lengths [Å] and angles [°] for CCDC # 840165.

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O(1)-C(1)	1.215(2)
O(2)-C(3)	1.215(2)
C(1)-C(13)	1.504(3)
C(1)-C(2)	1.530(3)
C(2)-C(3)	1.536(2)
C(2)-C(9)	1.566(2)
C(2)-H(2)	1.0000
C(3)-C(4)	1.523(3)
C(4)-C(5)	1.546(3)
C(4)-C(17)	1.564(3)
C(4)-H(4)	1.0000
C(5)-C(6)	1.503(3)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.341(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.511(3)
C(7)-C(16)	1.516(2)
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-C(10)	1.539(3)
C(9)-C(11)	1.541(3)
C(9)-C(14)	1.543(2)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-C(12)	1.525(3)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(13)	1.536(3)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-H(13A)	0.9900

C(13)-H(13B)	0.9900
C(14)-C(15)	1.546(3)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(15)-C(16)	1.565(3)
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(16)-C(17)	1.559(3)
C(16)-H(16)	1.0000
C(17)-C(19)	1.534(2)
C(17)-C(18)	1.539(3)
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800

O(1)-C(1)-C(13)	122.90(17)
O(1)-C(1)-C(2)	119.84(18)
C(13)-C(1)-C(2)	117.26(15)
C(1)-C(2)-C(3)	109.72(16)
C(1)-C(2)-C(9)	113.21(15)
C(3)-C(2)-C(9)	111.59(14)
C(1)-C(2)-H(2)	107.3
C(3)-C(2)-H(2)	107.3
C(9)-C(2)-H(2)	107.3
O(2)-C(3)-C(4)	120.79(17)
O(2)-C(3)-C(2)	121.12(17)
C(4)-C(3)-C(2)	118.06(15)
C(3)-C(4)-C(5)	111.93(14)
C(3)-C(4)-C(17)	113.59(15)
C(5)-C(4)-C(17)	110.06(16)
C(3)-C(4)-H(4)	107.0
C(5)-C(4)-H(4)	107.0
C(17)-C(4)-H(4)	107.0

C(6)-C(5)-C(4)	113.35(15)
C(6)-C(5)-H(5A)	108.9
C(4)-C(5)-H(5A)	108.9
C(6)-C(5)-H(5B)	108.9
C(4)-C(5)-H(5B)	108.9
H(5A)-C(5)-H(5B)	107.7
C(7)-C(6)-C(5)	124.94(16)
C(7)-C(6)-H(6)	117.5
C(5)-C(6)-H(6)	117.5
C(6)-C(7)-C(8)	120.30(17)
C(6)-C(7)-C(16)	122.69(18)
C(8)-C(7)-C(16)	116.78(16)
C(7)-C(8)-H(8A)	109.5
C(7)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(7)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(10)-C(9)-C(11)	109.94(16)
C(10)-C(9)-C(14)	111.03(16)
C(11)-C(9)-C(14)	107.28(14)
C(10)-C(9)-C(2)	107.12(15)
C(11)-C(9)-C(2)	110.38(15)
C(14)-C(9)-C(2)	111.13(15)
C(9)-C(10)-H(10A)	109.5
C(9)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(9)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(12)-C(11)-C(9)	113.32(15)
C(12)-C(11)-H(11A)	108.9
C(9)-C(11)-H(11A)	108.9
C(12)-C(11)-H(11B)	108.9
C(9)-C(11)-H(11B)	108.9
H(11A)-C(11)-H(11B)	107.7

C(11)-C(12)-C(13)	110.79(16)
C(11)-C(12)-H(12A)	109.5
C(13)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
C(13)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	108.1
C(1)-C(13)-C(12)	111.23(18)
C(1)-C(13)-H(13A)	109.4
C(12)-C(13)-H(13A)	109.4
C(1)-C(13)-H(13B)	109.4
C(12)-C(13)-H(13B)	109.4
H(13A)-C(13)-H(13B)	108.0
C(9)-C(14)-C(15)	121.57(15)
C(9)-C(14)-H(14A)	106.9
C(15)-C(14)-H(14A)	106.9
C(9)-C(14)-H(14B)	106.9
C(15)-C(14)-H(14B)	106.9
H(14A)-C(14)-H(14B)	106.7
C(14)-C(15)-C(16)	124.31(16)
C(14)-C(15)-H(15A)	106.3
C(16)-C(15)-H(15A)	106.3
C(14)-C(15)-H(15B)	106.3
C(16)-C(15)-H(15B)	106.3
H(15A)-C(15)-H(15B)	106.4
C(7)-C(16)-C(17)	111.16(15)
C(7)-C(16)-C(15)	115.17(15)
C(17)-C(16)-C(15)	118.70(16)
C(7)-C(16)-H(16)	103.1
C(17)-C(16)-H(16)	103.1
C(15)-C(16)-H(16)	103.1
C(19)-C(17)-C(18)	106.23(14)
C(19)-C(17)-C(16)	112.62(15)
C(18)-C(17)-C(16)	107.71(16)
C(19)-C(17)-C(4)	111.47(17)
C(18)-C(17)-C(4)	107.60(15)
C(16)-C(17)-C(4)	110.90(15)

C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(17)-C(19)-H(19A)	109.5
C(17)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(17)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

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Table S4. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for # 840165. The anisotropic displacement factor exponent takes the form:  $-2 \pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U11	U22	U33	U23	U13	U12
O(1)	16(1)	34(1)	28(1)	-5(1)	0(1)	-1(1)
O(2)	22(1)	20(1)	27(1)	3(1)	3(1)	2(1)
C(1)	18(1)	26(1)	19(1)	-2(1)	3(1)	-3(1)
C(2)	15(1)	18(1)	21(1)	-2(1)	2(1)	1(1)
C(3)	12(1)	20(1)	24(1)	1(1)	1(1)	-4(1)
C(4)	20(1)	22(1)	19(1)	1(1)	4(1)	0(1)
C(5)	17(1)	23(1)	23(1)	-3(1)	2(1)	0(1)
C(6)	19(1)	20(1)	22(1)	-3(1)	-2(1)	5(1)
C(7)	22(1)	21(1)	20(1)	-3(1)	0(1)	1(1)
C(8)	27(1)	26(1)	29(1)	4(1)	-1(1)	2(1)
C(9)	16(1)	20(1)	21(1)	0(1)	2(1)	0(1)
C(10)	20(1)	31(1)	23(1)	2(1)	2(1)	-2(1)
C(11)	19(1)	27(1)	25(1)	-5(1)	2(1)	3(1)
C(12)	26(1)	27(1)	31(1)	-11(1)	1(1)	4(1)
C(13)	24(1)	24(1)	36(1)	-8(1)	0(1)	-3(1)

C(14)	15(1)	23(1)	22(1)	0(1)	4(1)	0(1)
C(15)	16(1)	22(1)	25(1)	1(1)	0(1)	-2(1)
C(16)	19(1)	18(1)	23(1)	0(1)	0(1)	-1(1)
C(17)	19(1)	22(1)	19(1)	0(1)	-1(1)	2(1)
C(18)	23(1)	26(1)	22(1)	-3(1)	-1(1)	3(1)
C(19)	23(1)	25(1)	21(1)	-1(1)	-1(1)	3(1)

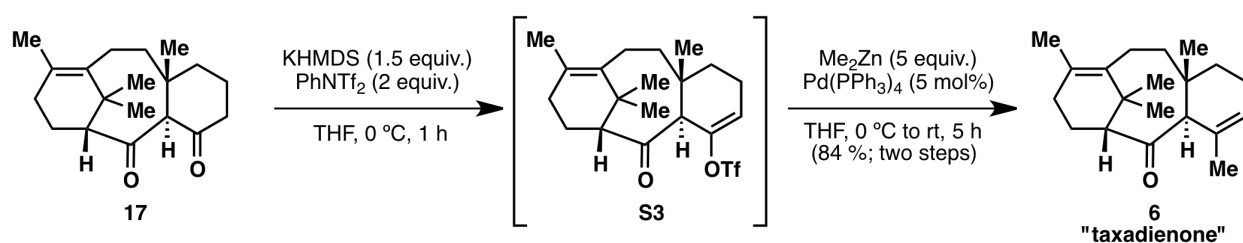
Table 5. Hydrogen coordinates ( $\times 10^4$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^{-3}$ ) for baran223.

	x	y	z	U(eq)
H(2)	8882	9628	2971	21
H(4)	8979	10519	-473	24
H(5A)	11050	9064	40	25
H(5B)	11108	9856	1455	25
H(6)	11050	7599	2037	25
H(8A)	9501	5963	2888	41
H(8B)	7818	5585	1919	41
H(8C)	7623	6399	3299	41
H(10A)	7816	9899	5480	37
H(10B)	7124	8654	4625	37
H(10C)	5800	9543	5394	37
H(11A)	5593	12238	3123	28
H(11B)	4813	11633	4458	28
H(12A)	7441	12046	5778	33
H(12B)	6693	13369	5105	33
H(13A)	8662	13282	3380	34
H(13B)	9747	13136	4837	34
H(14A)	5009	10385	1774	24
H(14B)	4074	9770	3020	24
H(15A)	4299	8190	1440	25
H(15B)	5528	7807	2751	25
H(16)	6374	7259	489	24
H(18A)	7115	7619	-1760	36



H(18B)	8979	7633	-935	36
H(18C)	8458	8758	-2021	36
H(19A)	5967	10134	-1658	35
H(19B)	5228	10274	-172	35
H(19C)	4778	9013	-1089	35

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**Enol Triflate (+)-S3 and Taxadienone (+)-6.** To a flame-dried 500 mL round-bottomed flask equipped with a stir bar were added *N*-phenylbis(trifluoromethanesulfonimide) (5.900 g, 16.51 mmol, 2.00 equiv) and 165 mL THF, and this solution was cooled to 0 °C. A dry solution of (+)-**17** (2.380 g, 8.252 mmol, 1.00 equiv) in THF (24 mL) was added, followed immediately by a 0.4 M solution (31 mL, 12.4 mmol, 1.50 equiv) of KHMDS in THF. This dark orange homogeneous solution was stirred for 1 h at 0 °C, after which it was quenched over a cold (0 °C) NaHCO<sub>3</sub> solution (300 mL, aqueous, saturated) in an Erlenmeyer flask. This mixture was then poured into a 2 L separatory funnel, diluted with hexanes (300 mL), and washed with aqueous KOH solution (3 N, 4 × 300 mL). The organic layers was washed further with 2 × 400 mL H<sub>2</sub>O and 2 × 400 mL brine, dried over MgSO<sub>4</sub> and evaporated to dryness *in vacuo* in a 500 mL round-bottomed flask. This crude material was carried on without purification to the next step.

The crude enol triflate from above was dissolved in 83 mL THF, and this solution was cooled to 0 °C. A solution of Pd(PPh<sub>3</sub>)<sub>4</sub> (477 mg, 0.413 mmol, 0.05 equiv with respect to amount of (+)-**17** added in the previous reaction) in 19 mL THF was added and stirred for 5 min at 0 °C,

to generate a yellow-orange solution. A solution of Me<sub>2</sub>Zn in PhMe (1.2 M, 34 mL, 40.8 mmol, 4.94 equiv) was added thereafter, and this yellow solution was stirred for 5 min at 0 °C before removing the ice bath and warming to room temperature over 5 h. After this time, the dark orange homogeneous solution was quenched with 100 mL HCl solution (1 N), and extracted with 2 × 200 mL hexanes. The organic layers were combined, washed with 30 mL H<sub>2</sub>O and 30 mL brine, dried over MgSO<sub>4</sub> and evaporated to dryness *in vacuo*. Purification via silica gel flash chromatography (gradient of EtOAc/hexanes) followed by crystallization from hot MeOH gave 1.9745 g of (+)-**6** (83.5 % yield over two steps).

Data for (+)-**S3**:

**Appearance:** Yellow liquid.

**TLC:**  $R_f$  = 0.41–0.43 (1:9 EtOAc/hexanes, very slightly UV active, does not stain with *p*-anisaldehyde staining but stains blue with ceric ammonium molybdate staining).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.94 (d,  $J$  = 6.8 Hz, 1 H), 3.62 (dt,  $J$  = 3.8, 1.8 Hz, 1 H), 2.70 – 2.64 (m, 1 H), 2.59 – 2.42 (m, 2 H), 2.33 – 2.14 (m, 3 H), 2.09 – 1.96 (m, 3 H), 1.91 (td,  $J$  = 13.9, 5.3 Hz, 1 H), 1.81 (s, 3 H), 1.39 (td,  $J$  = 12.8, 4.6 Hz, 1 H), 1.34 (ddd,  $J$  = 14.0, 3.5 Hz, 1 H), 1.19 (s, 3 H), 1.09 (s, 3 H), 0.97 (s, 3 H) ppm.

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>): δ 212.9, 149.5, 135.8, 131.7, 119.7, 118.5 (q,  $J$  = 320 Hz, CF<sub>3</sub>), 64.5, 55.2, 42.7, 40.1, 39.3, 38.4, 28.9, 28.0, 27.7, 23.3, 22.3, 20.3, 20.2, 17.8 ppm.

**IR** (neat):  $\tilde{\nu}$  = 2976, 2931, 2853, 1691, 1461, 1414, 1393, 1245, 1205 ( $\tilde{\nu}_{\text{max}}$ ), 1140, 1027, 938, 906, 888, 846 cm<sup>-1</sup>.

**HRMS** (ESI-TOF): calc'd for C<sub>20</sub>H<sub>27</sub>O<sub>4</sub>F<sub>3</sub>S [M + H<sup>+</sup>] 421.1655, found 421.1658.

**Optical rotation:**  $[\alpha]_D^{20}$  (c 0.43, CHCl<sub>3</sub>) = +18°.

Data for (+)-taxadienone (**6**):

**Appearance:** White solid that crystallises readily from MeOH/Et<sub>2</sub>O.

**Melting point:** 134–139 °C

**TLC:**  $R_f$  = 0.46–0.49 (1:9 EtOAc/hexanes, very slightly UV active and stains light purple upon *p*-anisaldehyde staining; stains blue with ceric ammonium molybdate staining).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): δ 5.55 (d,  $J$  = 6.1 Hz, 1 H), 3.30 (s, 1 H), 2.58 (t,  $J$  = 4.6 Hz, 1 H), 2.56 – 2.43 (m, 2 H), 2.25 (ddd,  $J$  = 15.4, 12.6, 3.8 Hz, 1 H), 2.20 – 2.04 (m, 2 H), 2.04 – 1.96 (m, 2 H), 1.86 – 1.74 (m, 2 H), 1.80 (s, 3 H), 1.48 (dq,  $J$  = 2.3, 1.1 Hz, 3 H), 1.36 – 1.27 (m, 2 H), 1.22 – 1.16 (m, 1 H), 1.20 (s, 3 H), 1.09 (s, 3 H), 0.91 (s, 3 H) ppm.

**<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>): δ 218.1, 136.9, 133.4, 130.7, 124.9, 65.0, 56.0, 43.6, 40.9, 38.6, 37.4, 29.0, 28.4, 27.7, 23.8, 23.7, 22.3, 21.9, 20.7, 18.8 ppm.

**IR** (neat):  $\tilde{\nu}$  = 2974, 2908, 2848, 1682 ( $\tilde{\nu}_{\text{max}}$ ), 1457, 1441, 1389, 1290, 1207, 1117, 1030, 930, 922, 849, 754 cm<sup>-1</sup>.

**HRMS** (ESI-TOF): calc'd for C<sub>20</sub>H<sub>30</sub>O [M + H<sup>+</sup>] 287.2369, found 287.2368.

**Optical rotation:**  $[\alpha]_D^{20}$  (c 0.27, CHCl<sub>3</sub>) = +52°.

X-ray crystallographic data for (+)-**6**:

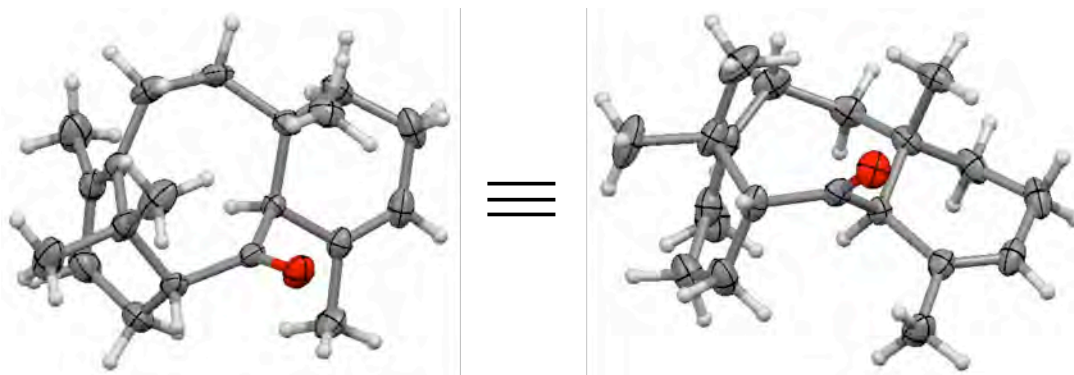


Table S6. Crystal data and structure refinement for CCDC # 837815.

Identification code	CCDC # 837815		
Empirical formula	C20 H30 O		
Formula weight	286.44		
Temperature	100(2) K		
Wavelength	1.54178 Å		
Crystal system	Orthorhombic		
Space group	P2(1)2(1)2(1)		
Unit cell dimensions	a = 9.8261(2) Å	α = 90°	
	b = 11.6102(2) Å	β = 90°	
	c = 14.6754(3) Å	γ = 90°	
Volume	1674.21(6) Å <sup>3</sup>		
Z	4		
Density (calculated)	1.136 g/cm <sup>3</sup>		
Absorption coefficient	0.507 mm <sup>-1</sup>		
F(000)	632		
Crystal size	0.36 x 0.34 x 0.30 mm <sup>3</sup>		
Theta range for data collection	4.86 to 68.18°		
Index ranges	-11 ≤ h ≤ 11, -12 ≤ k ≤ 13, -17 ≤ l ≤ 15		
Reflections collected	7309		
Independent reflections	2891 [R(int) = 0.0859]		
Completeness to theta = 65.00°	98.8 %		
Absorption correction	Multi-scan		
Max. and min. transmission	0.8628 and 0.8386		
Refinement method	Full-matrix least-squares on F <sup>2</sup>		
Data / restraints / parameters	2891 / 0 / 195		
Goodness-of-fit on F <sup>2</sup>	1.029		
Final R indices [I>2sigma(I)]	R1 = 0.0427, wR2 = 0.1119		
R indices (all data)	R1 = 0.0438, wR2 = 0.1127		
Absolute structure (Flack) parameter	0.0(3)		
Largest diff. peak and hole	0.197 and -0.205 e Å <sup>-3</sup>		

Table S7. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for CCDC # 837815.  $U(\text{eq})$  is defined as one third of the trace of the orthogonalised  $U_{ij}$  tensor.

	x	y	z	$U(\text{eq})$
O(1)	2169(1)	2158(1)	10057(1)	37(1)
C(1)	3707(2)	-2280(2)	8431(1)	50(1)
C(2)	4101(2)	-1273(1)	9025(1)	37(1)
C(3)	3565(2)	-1045(1)	9846(1)	33(1)
C(4)	4173(2)	-55(1)	10402(1)	38(1)
C(5)	4119(1)	1020(1)	9771(1)	33(1)
C(6)	2629(1)	1359(1)	9624(1)	27(1)
C(7)	1704(1)	748(1)	8923(1)	24(1)
C(8)	1148(2)	1703(1)	8304(1)	30(1)
C(9)	2188(2)	2509(2)	7906(1)	43(1)
C(10)	5108(2)	-457(2)	8593(1)	48(1)
C(11)	4955(2)	810(2)	8899(1)	44(1)
C(12)	-159(2)	1794(2)	8076(1)	38(1)
C(13)	-1229(2)	972(2)	8366(1)	43(1)
C(14)	-578(1)	-163(1)	8648(1)	36(1)
C(15)	569(1)	-43(1)	9361(1)	29(1)
C(16)	1050(2)	-1304(1)	9521(1)	35(1)
C(17)	2246(2)	-1597(1)	10153(1)	40(1)
C(18)	5675(2)	-308(2)	10665(2)	58(1)
C(19)	3450(2)	206(2)	11301(1)	49(1)
C(20)	-69(2)	461(1)	10232(1)	37(1)

Table S8. Bond lengths [Å] and angles [°] for CCDC # 837815.

O(1)-C(6)	1.2127(18)
C(1)-C(2)	1.509(2)
C(2)-C(3)	1.341(2)
C(2)-C(10)	1.509(2)
C(3)-C(17)	1.515(2)
C(3)-C(4)	1.531(2)
C(4)-C(19)	1.528(3)
C(4)-C(18)	1.553(2)
C(4)-C(5)	1.556(2)
C(5)-C(6)	1.5309(19)
C(5)-C(11)	1.540(2)
C(6)-C(7)	1.5449(18)
C(7)-C(8)	1.5338(19)
C(7)-C(15)	1.5813(18)
C(8)-C(12)	1.332(2)
C(8)-C(9)	1.504(2)
C(10)-C(11)	1.545(3)
C(12)-C(13)	1.483(3)
C(13)-C(14)	1.521(3)
C(14)-C(15)	1.544(2)
C(15)-C(20)	1.5390(19)
C(15)-C(16)	1.556(2)
C(16)-C(17)	1.535(2)
C(3)-C(2)-C(10)	120.73(15)
C(3)-C(2)-C(1)	124.84(16)
C(10)-C(2)-C(1)	114.30(16)
C(2)-C(3)-C(17)	121.31(14)
C(2)-C(3)-C(4)	118.27(15)
C(17)-C(3)-C(4)	119.56(14)
C(19)-C(4)-C(3)	115.28(15)
C(19)-C(4)-C(18)	105.37(16)
C(3)-C(4)-C(18)	111.18(14)
C(19)-C(4)-C(5)	109.81(13)

C(3)-C(4)-C(5)	105.77(12)
C(18)-C(4)-C(5)	109.39(14)
C(6)-C(5)-C(11)	115.68(13)
C(6)-C(5)-C(4)	108.84(12)
C(11)-C(5)-C(4)	110.41(13)
O(1)-C(6)-C(5)	118.64(13)
O(1)-C(6)-C(7)	118.72(12)
C(5)-C(6)-C(7)	122.61(12)
C(8)-C(7)-C(6)	105.80(11)
C(8)-C(7)-C(15)	114.15(11)
C(6)-C(7)-C(15)	114.27(11)
C(12)-C(8)-C(9)	120.55(15)
C(12)-C(8)-C(7)	123.36(14)
C(9)-C(8)-C(7)	115.97(12)
C(2)-C(10)-C(11)	114.27(15)
C(5)-C(11)-C(10)	116.40(14)
C(8)-C(12)-C(13)	124.08(16)
C(12)-C(13)-C(14)	109.73(12)
C(13)-C(14)-C(15)	114.40(13)
C(20)-C(15)-C(14)	107.45(12)
C(20)-C(15)-C(16)	110.84(13)
C(14)-C(15)-C(16)	103.83(12)
C(20)-C(15)-C(7)	113.85(11)
C(14)-C(15)-C(7)	106.96(12)
C(16)-C(15)-C(7)	113.15(11)
C(17)-C(16)-C(15)	122.17(12)
C(3)-C(17)-C(16)	112.43(13)

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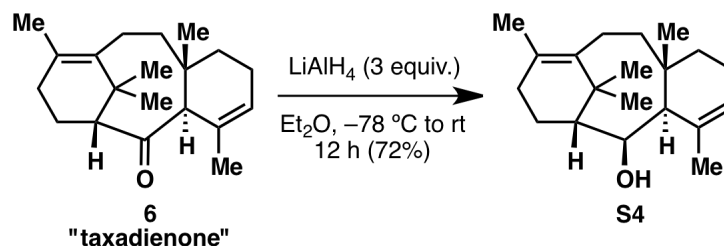
Table S9. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for CCDC # 837815. The anisotropic displacement factor exponent takes the form:  $-2 \pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U <sup>11</sup>	U <sup>22</sup>	U <sup>33</sup>	U <sup>23</sup>	U <sup>13</sup>	U <sup>12</sup>
O(1)	44(1)	27(1)	41(1)	-10(1)	-5(1)	2(1)
C(1)	47(1)	41(1)	61(1)	-19(1)	-3(1)	7(1)
C(2)	33(1)	29(1)	50(1)	-5(1)	-9(1)	6(1)
C(3)	37(1)	21(1)	42(1)	2(1)	-12(1)	4(1)
C(4)	43(1)	26(1)	44(1)	2(1)	-19(1)	1(1)
C(5)	29(1)	23(1)	46(1)	2(1)	-12(1)	-4(1)
C(6)	31(1)	19(1)	31(1)	2(1)	-2(1)	-2(1)
C(7)	23(1)	21(1)	27(1)	-2(1)	0(1)	1(1)
C(8)	34(1)	27(1)	28(1)	-3(1)	-2(1)	6(1)
C(9)	47(1)	35(1)	46(1)	13(1)	-3(1)	0(1)
C(10)	32(1)	51(1)	62(1)	-8(1)	5(1)	1(1)
C(11)	27(1)	40(1)	64(1)	5(1)	4(1)	-2(1)
C(12)	41(1)	37(1)	37(1)	-6(1)	-10(1)	15(1)
C(13)	26(1)	56(1)	48(1)	-17(1)	-6(1)	9(1)
C(14)	26(1)	41(1)	41(1)	-12(1)	2(1)	-7(1)
C(15)	27(1)	27(1)	32(1)	-5(1)	5(1)	-3(1)
C(16)	38(1)	23(1)	43(1)	-2(1)	4(1)	-10(1)
C(17)	55(1)	22(1)	42(1)	4(1)	-2(1)	-6(1)
C(18)	56(1)	41(1)	77(1)	-4(1)	-39(1)	7(1)
C(19)	75(1)	36(1)	36(1)	-1(1)	-19(1)	2(1)
C(20)	36(1)	41(1)	34(1)	-6(1)	11(1)	-5(1)



Table S10. Hydrogen coordinates ( $\times 10^4$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for CCDC # 837815.

	x	y	z	U(eq)
H(1A)	3194	-2840	8793	74
H(1B)	4530	-2645	8189	74
H(1C)	3141	-2007	7925	74
H(5)	4565	1668	10107	39
H(7)	2298	243	8540	29
H(9A)	1738	3051	7492	64
H(9B)	2871	2065	7569	64
H(9C)	2634	2937	8398	64
H(10A)	5003	-495	7923	58
H(10B)	6040	-721	8742	58
H(11A)	5876	1133	8993	52
H(11B)	4527	1246	8396	52
H(12)	-423	2426	7704	46
H(13A)	-1872	837	7858	52
H(13B)	-1745	1298	8884	52
H(14A)	-202	-542	8098	43
H(14B)	-1293	-672	8899	43
H(16A)	252	-1737	9749	42
H(16B)	1273	-1627	8915	42
H(17A)	2030	-1333	10778	48
H(17B)	2364	-2444	10172	48
H(18A)	6055	358	10987	87
H(18B)	6206	-454	10111	87
H(18C)	5711	-986	11061	87
H(19A)	2494	391	11180	73
H(19B)	3891	862	11599	73
H(19C)	3502	-470	11700	73
H(20A)	-332	1264	10123	56
H(20B)	594	428	10730	56
H(20C)	-877	12	10397	56



**Taxadien-2 $\beta$ -ol (+)-S4.** To a flame-dried 500 mL round-bottomed flask equipped with a stir bar was added a solution of (+)-**6** (1.974 g, 6.891 mmol, 1.00 eq) in Et<sub>2</sub>O (70 mL) and this solution was cooled to  $-78^\circ\text{C}$ . The septum atop the flask was briefly removed while solid LiAlH<sub>4</sub> (787 mg, 20.7 mmol, 3.00 eq) was added in 4 portions, and the septum was replaced immediately thereafter. The resulting grey slurry was then warmed to room temperature over 12 h. After this time, the reaction flask was cooled to  $0^\circ\text{C}$  and quenched slowly with H<sub>2</sub>O (100 mL). This mixture was then worked up with aqueous NaOH (3 N, 200 mL), H<sub>2</sub>O (300 mL), then extracted with 400 mL EtOAc. The layers were separated, and the aqueous layer was extracted with 2  $\times$  200 mL EtOAc. The organic layers were combined, washed with 400 mL H<sub>2</sub>O and 400 mL brine, dried over MgSO<sub>4</sub> and evaporated to dryness *in vacuo*. Purification via silica gel flash chromatography (gradient of EtOAc/hexanes) gave 1.435 g of (+)-**S4** (72.2 % yield). It is of note that yields greater than 80% could be achieved at the sub-gram scale.

**Appearance:** Colourless liquid

**TLC:**  $R_f$  = 0.43–0.46 (1:9 EtOAc/hexanes, very slightly UV active, stains dark blue upon *p*-anisaldehyde staining).

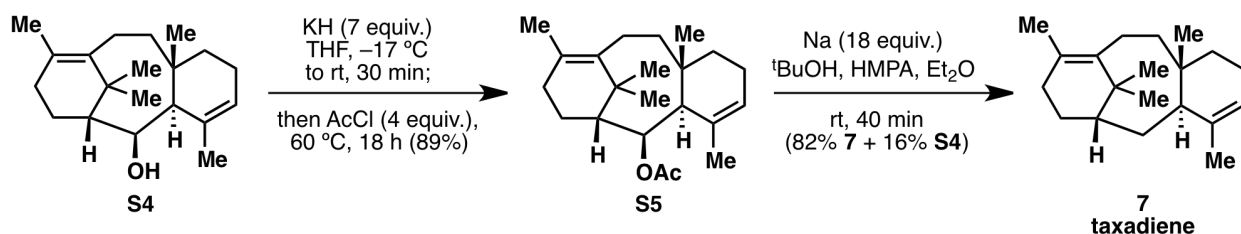
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>):  $\delta$  5.38 (s, 1 H), 4.49 (d,  $J$  = 3.9 Hz, 1 H), 2.88 (s, 1 H), 2.83 – 2.63 (m, 2 H), 2.37 – 2.24 (m, 1 H), 2.24 – 2.10 (m, 3 H), 2.08 – 2.01 (m, 1 H), 2.01 – 1.91 (m, 2 H), 1.82 (ddd,  $J$  = 18.4, 10.5, 3.3 Hz, 1 H), 1.79 (s, 3 H), 1.71 (s, 3 H), 1.64 (s, 3 H), 1.41 – 1.31 (m, 1 H), 1.30 – 1.19 (m, 2 H), 1.11 (dd,  $J$  = 11.6, 6.8 Hz, 1 H), 1.09 (s, 3 H), 1.08 (s, 3 H) ppm.

$^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  137.7, 137.5, 128.0, 122.4, 80.1, 51.7, 42.2, 40.3, 38.5, 38.2, 37.8, 32.7, 28.9, 26.4, 25.2, 25.1, 23.9, 23.8, 23.1, 21.2 ppm.

IR (neat):  $\tilde{\nu}$  = 3516, 3047, 3003, 2928 ( $\tilde{\nu}_{\text{max}}$ ), 2882, 2856, 1459, 1374, 1252, 1191, 1085, 1039, 921, 848, 794  $\text{cm}^{-1}$ .

HRMS (ESI-TOF): calc'd for  $\text{C}_{20}\text{H}_{32}\text{O}$  [ $\text{M} + \text{H}^+$ ] 289.2526, found 289.2522.

Optical rotation:  $[\alpha]_D^{20}$  (c 1.1,  $\text{CHCl}_3$ ) = +112°.



**2 $\beta$ -Acetoxytaxadiene (+)-S5 and Taxadiene (+)-7.** To a flame-dried 100 mL round-bottomed flask equipped with a stir bar was added potassium hydride (washed with hexanes and THF prior to use; 1.100 g, 27.43 mmol, 6.59 equiv) as a slurry in THF (4.0 mL), and this solution was cooled to  $-17\text{ }^{\circ}\text{C}$  (brine/dry ice). A solution of (+)-S4 (1.200 g, 4.160 mmol, 1.00 eq) in THF (6.0 mL) was added dropwise over 5 min, and this slurry was warmed to room temperature while stirring over 30 min. The reaction mixture was then re-cooled to  $-17\text{ }^{\circ}\text{C}$ , upon which freshly distilled acetyl chloride (1.20 mL, 1.325 g, 16.88 mmol, 4.06 equiv) was added dropwise, as the colour of the reaction mixture changes quickly from slightly yellow to dark orange. This mixture was then warmed to  $60\text{ }^{\circ}\text{C}$  while stirring over 18 h, after which TLC showed reaction completion. This brown slurry was cooled to  $0\text{ }^{\circ}\text{C}$ , and poured slowly while rinsing with hexanes (ca. 10 mL total) into a cooled ( $0\text{ }^{\circ}\text{C}$ ), vigorously stirred solution of hexanes (50 mL) and aqueous hydrochloric acid (0.5 N; 50 mL) in a 500 mL Erlenmeyer flask. This mixture was then warmed to room temperature while vigorously stirring over 30 min. The resulting layers were

then separated, and the aqueous layer was extracted with  $2 \times 40$  mL 1:3 EtOAc/hexanes. The organic layers were combined, washed with 100 mL H<sub>2</sub>O and 100 mL brine, dried over MgSO<sub>4</sub> and evaporated to dryness *in vacuo*. Purification via silica gel flash chromatography (slow gradient from hexanes to 1:40 EtOAc/hexanes) gave 1.220 g of (+)-**S5** (88.7 % yield).

To a flame-dried 250 mL round-bottomed flask equipped with a stir bar were added freshly distilled HMPA (from CaH<sub>2</sub>; 10 mL) and dry Et<sub>2</sub>O (5 mL), and this solution was degassed. Freshly sliced sodium metal (washed with degassed hexanes then degassed Et<sub>2</sub>O; 2.00 g, 66.1 mmol, 18.2 eq) was then added, and the reaction mixture was degassed for 10 min with a stream of argon, over which time the solution became dark blue. A degassed solution of (+)-**S5** (1.200 g, 3.631 mmol, 1.00 eq) in 1:1 <sup>t</sup>BuOH/Et<sub>2</sub>O (8 mL) was then prepared, and was added slowly to the blue reaction mixture over the course of 40 min, being careful not to decolourize the blue solution (the dark blue solution becomes lighter every time the substrate is added but never goes fully colourless; the reaction mixture regenerates the dark blue colour within a few minutes). After the addition was complete and the reaction mixture regained its blue colour, the flask was opened to air and the reaction mixture was transferred via Pasteur pipet to a cooled (0 °C), vigorously stirred 100 mL Erlenmeyer flask containing aqueous hydrochloric acid (0.5 N; 10 mL). The remaining sodium metal should NOT be transferred. The reaction flask was rinsed with  $2 \times 10$  mL Et<sub>2</sub>O, and this rinsate added to the Erlenmeyer flask as well. This mixture was then warmed to room temperature while vigorously stirring over 30 min. The resulting layers were then separated, and the aqueous layer was extracted with  $2 \times 30$  mL hexanes. The organic layers were combined, washed with 40 mL H<sub>2</sub>O and 40 mL brine, dried over MgSO<sub>4</sub> and evaporated to dryness *in vacuo*. Loading the crude mixture onto a silica gel plug and eluting with hexanes gave 0.811 g of (+)-**7** (81.9 % yield), and eluting with 1:9 EtOAc/hexanes gave 0.163 g of deacetylated product (+)-**S4** (15.6 % yield).

Data for (+)-**S5**:

**Appearance:** Colourless oil that solidifies to an amorphous white solid upon high vacuum

**TLC:**  $R_f = 0.54\text{--}0.56$  (1:9 EtOAc/hexanes, not UV active, stains blue upon *p*-anisaldehyde staining).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.60 (d,  $J = 4.0$  Hz, 1 H), 5.30 (s, 1 H), 3.05 (s, 1 H), 2.77 (td,  $J = 13.5, 5.0$  Hz, 1 H), 2.64 (td,  $J = 14.3, 4.9$  Hz, 1 H), 2.35 – 2.23 (m, 1 H), 2.23 – 2.06 (m, 3 H), 2.03 (s, 3 H), 2.03 – 1.89 (m, 3 H), 1.82 (ddd,  $J = 18.3, 10.4, 3.3$  Hz, 1 H), 1.76 (s, 3 H), 1.69 (s, 3 H), 1.50 (s, 3 H), 1.41 – 1.31 (m, 2 H), 1.16 – 1.08 (m, 1 H), 1.02 (s, 3 H), 0.96 (s, 3 H) ppm.

**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.0, 137.6, 137.0, 128.8, 122.1, 79.7, 47.8, 41.2, 40.4, 38.5, 38.3, 37.9, 32.5, 29.0, 26.1, 25.3, 24.5, 24.1, 23.9, 22.5, 21.8, 21.4 ppm.

**IR** (neat):  $\tilde{\nu} = 3051, 3006, 2883, 1733, 1459, 1376, 1362, 1232$  ( $\tilde{\nu}_{\text{max}}$ ), 1117, 1081, 1035, 1021, 947, 935, 786  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF): calc'd for  $\text{C}_{22}\text{H}_{34}\text{O}_2$   $[\text{M} + \text{H}^+]$  331.2631, found 331.2632.

**Optical rotation:**  $[\alpha]_D^{20}$  (c 1.0,  $\text{CHCl}_3$ ) = +85°.

Data for (+)-taxadiene (**7**).

**Appearance:** Colourless, viscous liquid

**TLC:**  $R_f = 0.52\text{--}0.55$  (hexanes, very slightly UV active, stains dark blue upon *p*-anisaldehyde staining).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.29 (bs, 1 H), 2.62 (ddd,  $J = 14.8, 10.1, 5.2$  Hz, 1 H), 2.52 (bs, 1 H), 2.37 – 2.25 (m, 1 H), 2.20 – 2.11 (m, 1 H), 2.11 – 1.96 (m, 2 H), 1.94 – 1.83 (m, 2 H), 1.81 (ddd,  $J = 14.8, 10.2, 4.7$  Hz, 1 H), 1.77 – 1.72 (m, 1 H), 1.72 – 1.62 (m, 2 H), 1.68 (s, 3 H), 1.66 (s, 3 H), 1.62 – 1.55 (m, 2 H), 1.42 (ddd,  $J = 14.9, 6.4, 5.4$  Hz, 1 H), 1.33 (s, 3 H), 1.19 (dd,  $J = 12.7, 6.1$  Hz, 1 H), 1.03 (s, 3 H), 0.83 (s, 3 H) ppm.

**$^{13}\text{C}$  NMR** (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.7, 137.8, 129.7, 121.3, 44.4, 41.5, 39.9, 39.2, 38.6, 37.5, 30.9, 29.9, 28.5, 26.4, 24.6, 24.2, 23.3, 22.8, 21.8, 21.6 ppm.

**IR** (neat):  $\tilde{\nu}$  = 2952, 2930 ( $\tilde{\nu}_{\text{max}}$ ), 2926, 2850, 1458, 1442, 1387, 1375, 1330, 1109, 1084, 1028, 966, 833, 822  $\text{cm}^{-1}$ .

**HRMS** (ESI-TOF): calc'd for  $\text{C}_{20}\text{H}_{32}$  [ $\text{M} + \text{H}^+$ ] 273.2577, found 273.2585.

**Optical rotation:**  $[\alpha]_D^{20}$  (c 1.0,  $\text{CHCl}_3$ ) = +165°;  $[\alpha]_D^{20}$  (c 0.32,  $\text{CHCl}_3$ ) = +170°.

The spectroscopic data for this compound were identical to those reported in Croteau and co-workers, *J. Biol. Chem.* **1995**, 270, 8686–8690 and Williams and co-workers, *J. Org. Chem.* **1995**, 60, 7215–7223.

Table S11. Comparison of  $^1\text{H}$  NMR data for taxadiene (**7**), compiled in decreasing order of chemical shift ( $\delta$ ).

Synthetic (+)-taxadiene ( <b>7</b> ) <i>This manuscript</i> $^1\text{H}$ NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ (multiplicity, $J$ , # of H)	Natural taxadiene ( <b>7</b> ) <i>J. Biol. Chem.</i> <b>1995</b> , 270, 8686 $^1\text{H}$ NMR ( $\text{CDCl}_3$ , 500 MHz) $\delta$ (# of H); other parameters are not specified	Synthetic taxadiene ( <b>7</b> ) <i>J. Org. Chem.</i> <b>1995</b> , 60, 7215 $^1\text{H}$ NMR ( $\text{CDCl}_3$ , 300 MHz) $\delta$ (multiplicity, $J$ , # of H)
5.29 (bs, 1 H)	5.28 (1 H)	5.27 (m, 1 H)
2.62 (ddd, $J$ = 14.8, 10.1, 5.2 Hz, 1 H)	2.61 (1 H)	2.6 (ddd, $J$ = 14.8, 10.0, 5.2 Hz, 1 H)
2.52 (bs, 1 H)	2.51 (1 H)	2.5 (bs, 1 H)
2.37 – 2.25 (m, 1 H)	2.31 (1 H)	2.38 – 2.21 (m, 1 H)
2.20 – 2.11 (m, 1 H)	2.15 (1 H)	2.2 – 1.95 (m, 3 H)
2.11 – 1.96 (m, 2 H)	2.08 (1 H)	
	2.01 (1 H)	
1.94 – 1.83 (m, 2 H)	1.88 (1 H)	1.95 – 1.55 (m, 8 H)
	1.88 (1 H)	
1.81 (ddd, $J$ = 14.8, 10.2, 4.7 Hz, 1 H)	1.82 (1 H)	
1.77 – 1.72 (m, 1 H)	1.74 (1 H)	
1.72 – 1.62 (m, 2 H)	1.67 (1 H)	
	1.66 (1 H)	

1.68 (s, 3 H)	1.68 (3 H)	1.69 (s, 3 H)
1.66 (s, 3 H)	1.66 (3 H)	1.68 (s, 3 H)
1.62 – 1.55 (m, 2 H)	1.59 (1 H)	-- included in above --
	1.57 (1 H)	
1.42 (ddd, $J = 14.9, 6.4, 5.4$ Hz, 1 H)	1.42 (1 H)	1.4 (ddd, $J = 14.8, 5.5, 5.5$ Hz, 1 H)
1.33 (s, 3 H)	1.33 (3 H)	1.31 (s, 3 H)
1.19 (dd, $J = 12.7, 6.1$ Hz, 1 H)	1.18 (1 H)	1.18 (dd, $J = 12.7, 6.0$ Hz, 1 H)
1.03 (s, 3 H)	1.01 (3 H)	1.0 (s, 3 H)
0.83 (s, 3 H)	0.82 (3 H)	0.8 (s, 3 H)

Table S12. Comparison of  $^{13}\text{C}$  NMR data for taxadiene (**7**), compiled in decreasing order of chemical shift ( $\delta$ ).

Synthetic taxadiene ( <b>7</b> ) <i>This manuscript</i> $^{13}\text{C}$ NMR ( $\text{CDCl}_3$ , 151 MHz) $\delta$ (# of H determined via APT NMR)	Natural taxadiene ( <b>7</b> ) <i>J. Biol. Chem.</i> <b>1995</b> , 270, 8686 $^{13}\text{C}$ NMR ( $\text{CDCl}_3$ , 126 MHz) $\delta$ (# of H determined via DEPT NMR)	Synthetic taxadiene ( <b>7</b> ) <i>J. Org. Chem.</i> <b>1995</b> , 60, 7215 $^{13}\text{C}$ NMR ( $\text{CDCl}_3$ , 75 MHz) $\delta$ (# of H not determined)
138.7 ( $\text{C}_q$ )	138.5 ( $\text{C}_q$ )	138.5
137.8 ( $\text{C}_q$ )	137.7 ( $\text{C}_q$ )	137.7
129.7 ( $\text{C}_q$ )	129.5 ( $\text{C}_q$ )	129.5
121.3 (CH)	121.1 (CH)	121.1
44.4 (CH)	44.2 (CH)	44.3
41.5 ( $\text{CH}_2$ )	41.4 ( $\text{CH}_2$ )	41.4
39.9 (CH)	39.7 (CH)	39.8
39.2 ( $\text{C}_q$ )	39.0 ( $\text{C}_q$ )	39.0
38.6 ( $\text{CH}_2$ )	38.5 ( $\text{CH}_2$ )	38.5
37.5 ( $\text{C}_q$ )	37.2 ( $\text{C}_q$ )	37.3
30.9 ( $\text{CH}_3$ )	30.7 ( $\text{CH}_3$ )	30.7
29.9 ( $\text{CH}_2$ )	29.8 ( $\text{CH}_2$ )	29.8
28.5 ( $\text{CH}_2$ )	28.4 ( $\text{CH}_2$ )	28.4
26.4 ( $\text{CH}_3$ )	26.3 ( $\text{CH}_3$ )	26.3
24.6 ( $\text{CH}_2$ )	24.5 ( $\text{CH}_2$ )	24.5
24.2 ( $\text{CH}_3$ )	24.0 ( $\text{CH}_3$ )	23.9
23.3 ( $\text{CH}_2$ )	23.2 ( $\text{CH}_2$ )	23.2
22.8 ( $\text{CH}_2$ )	22.6 ( $\text{CH}_2$ )	22.6
21.8 ( $\text{CH}_3$ )	21.6 ( $\text{CH}_3$ )	21.6
21.6 ( $\text{CH}_3$ )	21.5 ( $\text{CH}_3$ )	21.5

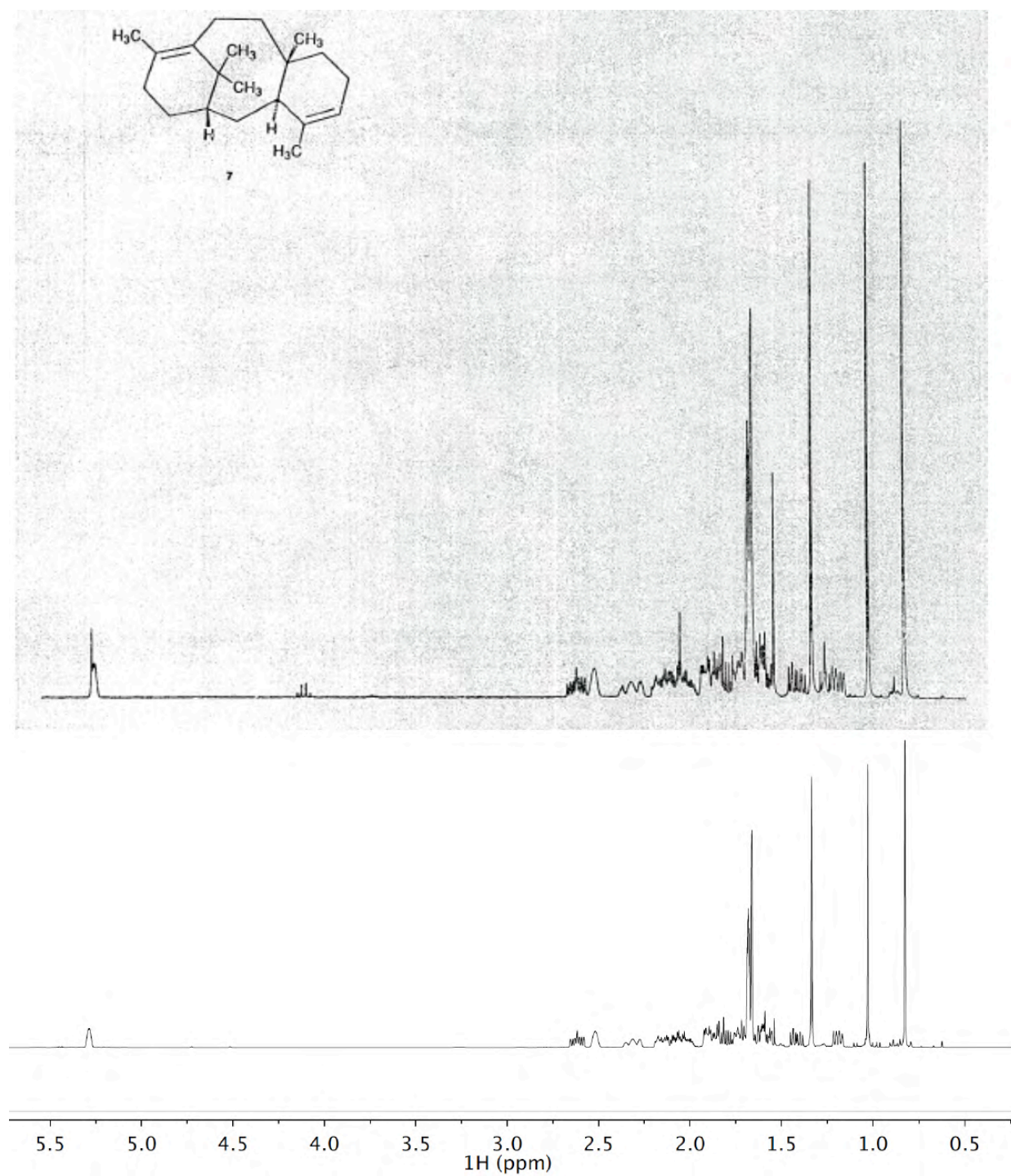


Figure S4. Overlaid spectra of synthetic taxadiene (**7**) from this manuscript (below, CDCl<sub>3</sub>, 400 MHz) to that of Williams and co-workers, *J. Org. Chem.* **1995**, *60*, 7215–7223 (above, CDCl<sub>3</sub>, 300 MHz).



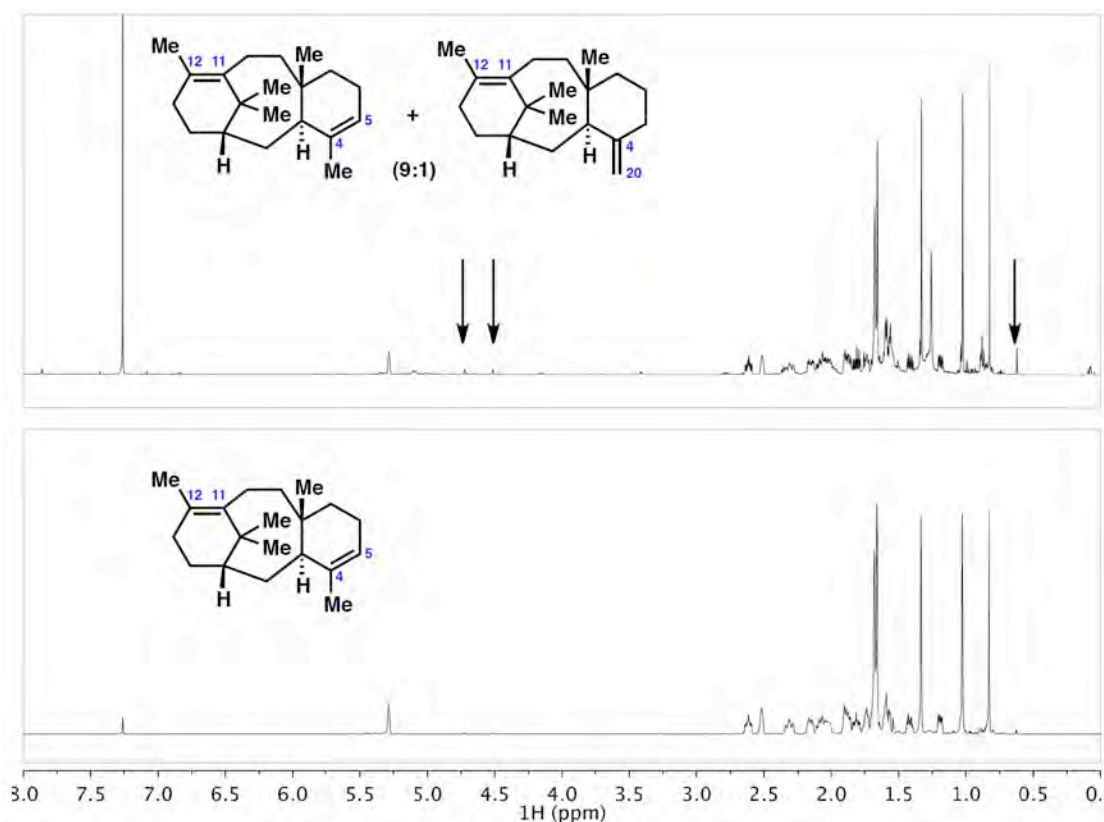


Figure S5. Overlaid spectra of synthetic taxadiene (**7**) from this manuscript (below,  $\text{CDCl}_3$ , 600 MHz) to that generated by bioengineering, obtained from Professor Gregory Stephanopoulos, cf. *Science* **2010**, 330, 70–74 (above,  $\text{CDCl}_3$ , 600 MHz). Note: Professor Stephanopoulos' taxadiene sample was freed of solvent and polar impurities before acquiring this spectrum; however, taxadiene produced via cell culture is a 9:1 mixture of taxa-4(5),11(12)-diene and taxa-4(20),11(12)-diene (its prominent features are depicted via arrows).

The optical rotation for this compound has hitherto not been reported. Taxadiene (**7**) obtained from Professor Gregory Stephanopoulos' bioengineered cell-culture production has been purified and its optical rotation has been measured for comparison:

Bioengineered taxadiene (**7**):  $[\alpha]_D^{20}$  (c 0.32,  $\text{CHCl}_3$ ) = +135°.

Synthetic taxadiene (**7**):  $[\alpha]_D^{20}$  (c 0.32,  $\text{CHCl}_3$ ) = +170°.